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Role of mental-psychological health as a modifiable factor in prevention of osteoarthritis pain flares: An extension to leap study

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ABSTRACT

Objective: We examined the correlation between osteoarthritis (OA) pain and mental health. Methods: Two hundred sixty-six participants were interviewed weekly for 12 weeks from May 2021 - August 2021, with the WOMAC pain subscale and the 5-item Mental Health Inventory being measured (MHI-5). We used linear regression to investigate correlations controlling for age, gender, body mass index, and medication usage. To account for the correlation between repeated measurements, generalized estimating equations were employed. In a case crossover study, we also used conditional logistic regression to examine the relationship between MHI-5 and the probability of pain flare. Ethical approval was obtained from KSUMC number (# LP-178929). *Results*: There were 75 males and 191 women in all. The average age was 65.0, the average BMI was 31.5, and 82 percent had knee as their main location. The mean WOMAC score in the quartile was 2.93 Vs 4.57 (p for trend across quartiles 0.001). In the case crossover study (91 participants), the poorest MHI-5 quartile had 2.1 times the chances of a pain flare the following week as the best MHI-5 quartile (p0.001). *Conclusion*: We found a link between poorer mental health indicators, OA pain, and the likelihood of pain flares. General mental health is a controllable component of health that may offer a novel approach to preventing OA pain flares.

Keywords: osteoarthritis; pain; mental health

1. INTRODUCTION

Osteoarthritis (OA) is a widespread and severe disease that affects about 12% of people aged 25 to 74 years (Lawrence et al., 1998), with over 27 million individuals in the United States suffering from clinical OA of any joint (Lawrence et al., 2008). This disease is linked to the overwhelming majority of hip and knee replacement operations, with societal expenses in the United States approaching $15 billion each year (Felson & Zhang, 1998). Furthermore, pain intensity levels seem to fluctuate within an individual (Hill et al., 2001)

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over both long and short time periods (Gooberman-Hill et al., 2007), which patients attribute to a variety of variables including weather, activity level, and medication usage. There has been little study done on defining or describing short-term changes in pain level in OA, (Bellamy et al., 1990) and the sources of pain in individuals with radiographic OA are unknown (Baker & Kirsch, 1991). Pain is a complex disease (Bates et al., 1993) with many components and measuring problems. Nociception, (Diatchenko et al., 2006) neuropathic symptoms, (Diatchenko et al., 2005) psychological and personality variables, (Dickens et al., 2003) genetic influences, (Einarsdottir et al., 2004) previous painful experiences, comorbid diseases, and pain expectancies all contribute to or modify the sensation of pain (Salaffi et al., 2003). We used a case crossover analysis to compare case and control periods within a single subject to try to minimize some of the between-subject issues in pain assessment (Barrett et al., 1987).

Depression is also a prevalent illness, with a frequency of 16% among the elderly (Oxman et al., 1990) and a disability effect similar to other major diseases such as heart disease and hypertension (Wells et al., 1989). In patients with OA, psychological well-being has been shown to be substantially related with disability, (van Baar et al., 1998) and anxiety has been reported to be connected with knee pain in women (Creamer et al., 1999).

Depression treatment has also been shown to reduce arthritis pain levels (Creamer et al., 1998). Too far, no longitudinal research has investigated changes in OA pain (Creamer et al., 2000) and their relationship to changes in general mental health (Lin et al., 2003). We looked at the connection between self-rated pain variations on a weekly basis and health outcomes such as healthcare resource usage in individuals with hip and/or knee osteoarthritis (Hutchings et al., 2007). We examined the impact of mental health variables in OA pain variations using comprehensive information from these weekly interviews on mental health factors.

2. MATERIALSAND METHODS

A more comprehensive explanation of the LEAP research may be found elsewhere (Hutchings et al., 2007). In summary, participants in the LEAP trial were recruited from general care and rheumatology practices throughout the United States who had clinical diagnoses of hip or knee OA as determined by their own doctors. The LEAP trial enrolled participants by selecting locations in the United States with a high proportion of OA patients. Posters were placed in the offices, and both the practices and the patients were compensated for recruitment and participation. The participants took part in telephone interviews at one-week intervals for up to 12 weeks, from May 2021- August 2021, during which they answered questions regarding their OA pain, psychological status, and a range of other topics. Medication usage was tracked by noting how many days in the preceding week participants used either prescription or over-the-counter medicines to manage their discomfort. Ethical approval was obtained from KSUMC number (# LP-178929).

Pain Assessment

The WOMAC pain subscale score was used as an outcome measure (0-10 scale). This scale indicates greater pain at the upper end of the scale and was determined by the question "Thinking about the pain you felt in your signal joint> due to your OA in the past week." Please rate your discomfort on a scale of 0 (no pain) to 10 (very painful) (extreme pain). How much discomfort do you feel... Is it possible to walk on a level surface? Are you going up or down the stairs? While lying in bed at night? Should you sit or lie? “Are you standing straight?” For this study, the overall score of 50 was standardized to a 0-10 scale. The WOMAC was assessed at baseline and at weekly intervals, with a weekly average produced in each instance.

Mental Health Status Assessment

The LEAP research gathered the Mental Health Index-5 (MHI-5) on a weekly basis. The MHI-5 evaluates overall mood or affect as well as positive well-being and measures general mental health (Berwick et al., 1991). It has also been shown to be reliable for screening for mood disorders (Hoeymans et al., 2004). In this study, we present raw scores (scale 5-30), with lower scores indicating poorer mental health. The MHI-5 has questions such as, "How much of the time were you a cheerful person in the last week?" with responses on a 6-point Likert scale ranging from "all of the time" to "none of the time." The MHI-5 is a validated general mental health assessment (Rumpf et al., 2001).

Statistical Analysis

In order to investigate the short-term relationship between mental health and pain, we eliminated data when the time gap between two consecutive interviews was more than 8 days. We also conducted sub-analyses with either shorter or longer time periods. SPSS statistical software, version 9.1, was used to conduct the analyses (SPSS Institute, Inc.).

We looked at the relationship between MHI-5 and the change in WOMAC discomfort one week later. We classified baseline

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MHI-5 and the change from baseline to the value one week prior to the WOMAC score under consideration as quartiles. There is no universally agreed-upon or clinically verified cutpoint for a case of common mental illness in the MHI-5. We used Hoeymans' cutpoint for high prevalence of mental health issues of 72 (or 23 points on the raw scale we use) as our cutpoint, and the first quartile in our research corresponds to MHI-5 scores that are less than this amount.

As a result, our analyses revealed four quartiles, the first of which included MHI-5 values representing a population with a high prevalence of mental health problems, and the other three representing three ordinal categories within a population of subjects with MHI-5 values associated with a low prevalence of mental health problems. We adjusted for age, gender, body mass index, and prescription and over-the-counter pain medication use (defined as whether the subject used prescription/over-the-counter pain medication to treat pain in the previous week, and if so, how many days each type was used) in a multiple linear regression model. The dependent variable was WOMAC pain, while the independent factors were baseline MHI-5 quartiles and MHI-5 score change. To account for correlated data from repeated measurements within a subject, we utilized generalized estimating equations.

Using a conditional logistic regression model, we also performed a case crossover study to evaluate the relationship between overall mental health and the likelihood of pain flare one week later. As the unit of analysis, we utilized each weekly time point for each topic. A “pain flare” (or “case period”) was defined as an interview in which the patient reported a WOMAC score in the top thirty percent of all WOMAC scores. A "control period" was defined as an interview in which the respondent reported a WOMAC score in the bottom seventy percent of all WOMAC scores. This study included only individuals who had at least one case period and at least one control period.

3. RESULTS

In the LEAP research, 353 individuals were assessed, 288 were recruited, 9 subjects had no pain information gathered, and 7 had just one visit with pain information recorded. A further six patients had a time span of more than eight days between all visits, and they were excluded from the study. Restricting the analysis to visits with a previous visit of 8 days or fewer removed 14% of the total visits while maintaining close closeness between putative predictors and the WOMAC pain result. In addition, a small number of patients (23) had individual visits that were presumably filled out with reference to discomfort in a joint other than their "signal joint"; these visits were excluded from the analysis.

The analytic group comprised 266 patients, all of whom had a clinical diagnosis of OA of the hip, knee, or both, as determined by the original LEAP investigators. Sixty-seven percent of the participants were recruited from rheumatology clinics, whereas 33 percent were recruited from general practice clinics. There were 75 males and 191 women among these individuals, with a mean age of 65.0 (SD8.5) and a mean BMI of 31.5 (SD7.4) (Table 1).

Table 1 Subject Characteristics

Characteristic	Subjects (n=266)	Case-crossover Subjects (n=91)
Age, years [mean (SD)]	65(±8.5)	65(±8.8)
Female [n (%)]	191 (71)	72 (79)
BMI, kg/m2 [mean (SD)]	31.5 (±7.4)	31.4 (±8.8)
Race – Non-Hispanic White	89%	89%
Race – African-American	6%	8%
Race – Other	5%	3%
Knee as primary site [n (%)]	216 (82)	71 (78)
Hip as primary site [n (%)]	50 (18)	20 (22)
WOMAC range	0.2-9.6	0.2-4.9 (control periods) 5.0-9.6 (case periods)
WOMAC [mean (SD)]	3.8 (±2.2)	4.5 (±1.8)
MHI-5 [mean (SD)]	25.1 (±4.0)	24.7 (±4.0)

The knee was the main site of OA in 82 percent of the patients, whereas the hip was the primary site in 18 percent. Radiographs indicated OA in the signal joint in 80% of the patients, whereas radiographs were unavailable in 20%. The WOMAC score range was broad, ranging from 0.2 to 9.6, with a mean for the whole group of 3.8 (2.2). MHI-5 was 25.1 (4.0) on average. According to Hutchings (22), the majority of individuals completed the majority of repeated measures, with a mean number of follow-ups completed of 10.7 out of a possible 12. 12 to 82 percent of participants completed ten or more interviews.

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GEE Results

As demonstrated in Table 2 and Figure 1, higher baseline mental health was related with less pain than poor baseline mental health (adjusted mean WOMAC score 2.93 for the highest quartile of MHI-5 vs 4.57 for the lowest quartile; p for trend0.001). Changes in MHI-5 from baseline were likewise linked to changes in WOMAC pain (Table 2 and Figure 2). The quartile with the most improvement from baseline in mental health had higher WOMAC scores than the quartile with the greatest deterioration from baseline, with an adjusted mean WOMAC score of 3.53 for the highest MHI-5 quartile compared to 4.06 for the lowest quartile (p for trend0.001). We observed comparable findings whether we restricted the analysis to time periods longer or shorter than 8 days.

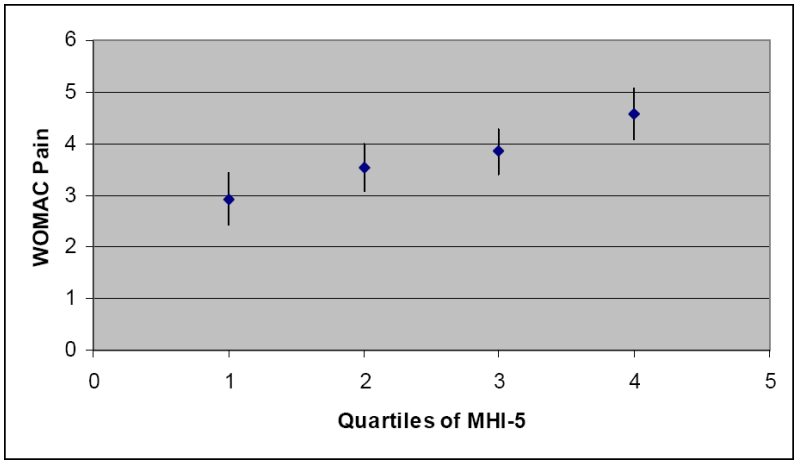

Figure1 Baseline MHI-5 in quartiles with mean WOMAC pain, adjusted for age, sex, BMI, andmedication use. p for trend <0.001. The first quartile is those with the best mental health, while the fourth quartile represents those with the worst mental health. Error bars represent 95% confidence intervals.

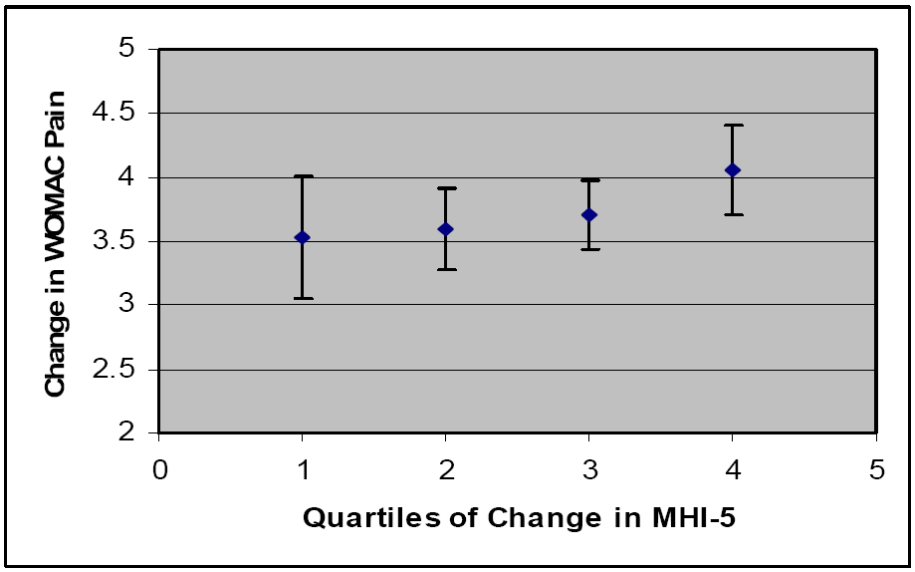

Figure 2 Change in MHI-5 with mean change in WOMAC pain, adjusted for age, sex, BMI, andmedication use. p for trend <0.001. Error bars represent 95% confidence intervals.

Table 2 Relation of MHI-5 and its change to pain intensity, adjusted for age, sex, BMI, and medication use (linearregression model)

MHI-5	N Observations	Adjusted Mean WOMAC Pain
Baseline MHI-5 Values		
28-30	53	2.93
26-27	67	3.54
23-25	75	3.86

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13-22	68	4.57
Pfor trend		<0.001
Change of MHI-5		
3-14 (improved)	448	3.53
1-2	517	3.59
0-0	556	3.71
(-13) – (-1) (worsened)	526	4.06
P for trend		<0.001

Case Crossover Results

The case crossover analysis comprised 91 individuals, who were the only ones out of 266 who had both at least one case period and at least one control period. These individuals' demographic features matched those of the entire sample (Table 1). The WOMAC range was 0.2-4.9 for control periods and 5.0-9.6 for case periods, with a mean WOMAC score of 4.5 (1.8) and a mean MHI-5 of 24.7 (4.0). The likelihood of pain flare was linked to general mental wellbeing. Table 3 shows that when individuals had the lowest MHI-5 scores, the chances of a pain flare the next week were 2.11 times greater than when the same subjects were in periods with the highest MHI-5 scores (p0.001).

Table 3 MHI-5 and its relation to pain flares (case crossover analysis) Adjusted for medication use.

MHI-5 Quartile Range	N Case Periods	N Control Periods	Unadjusted Odds Ratio	Adjusted Odds Ratio
28-30 (ref)	77	143	1.00	1.00
26-27	68	89	1.18	1.19
23-25	89	86	2.05	1.95
13-22	102	95	2.01	2.11
P for trend			0.002	<0.001

4. DISCUSSION

In summary, in a cross-sectional study, worse baseline mental health is linked with worse OA knee pain. Furthermore, increase in mental health from baseline is linked to decreased OA pain. Finally, poorer mental health in the week before the flare increases the chance of a pain flare. These three fundamental results point to a significant correlation and potentially predictive relationship between mental health and OA pain. There are many reasons for investigating mental health issues and their relationship to pain in OA. First, it is evident that the etiology of OA pain is poorly understood, and that both peripheral and central neuronal function impairments may be involved (Kelly et al., 2008). Given the central nervous system's significance in comprehending pain, and the established relationship between depressions or other components of mental health and intrinsic neuronal function, psychological variables become prominent candidates as mediators of pain perception (Schaible et al., 2002).

Second, pain in a number of different diseases has been linked to psychological state, and antidepressant therapy has been shown to reduce pain. Tricyclic antidepressants have been shown in small trials to be effective at reducing pain in rheumatoid arthritis patients, (Ash et al., 1999) but have not gained widespread use for the treatment of that disease due to the development of disease-modifying drugs for that condition; there are currently no disease-modifying treatments for OA (Frank et al., 1988). Three recent meta-analyses of fibromyalgia antidepressant therapy have all confirmed the probability of a moderate impact on pain with tricyclics, while duloxetine has shown a substantial and recurrent effect on sensitive points and pain measures in randomized, controlled clinical trials (Sarzi et al., 1988). Finally, there is some early evidence that depression therapy, a strong component in mental health, may improve pain in OA; a substantial decrease in OA pain in OA patients with improved therapy for coexisting depression (Arnold et al., 2000).

The intrinsic strengths of the original LEAP data are carried over into our research. These include, to the best of our knowledge, the first weekly independent assessments of pain and mental health in an OA patient group, A change of 10 points in the Nettles paper corresponds to a change of 2.5 points on the raw MHI-5 scale used in this paper, which is much smaller than the change values observed in the LEAP study (O'Malley et al., 2000). Our research obviously has major limitations. Combining hip and knee OA patients into a single cohort is one of them. Our most important drawback, however, is inherent in every research of pain and mental health: it is extremely difficult to address the issue of reverse causality in these data. It is possible, as we have discovered

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that mental health influences pain levels in OA. However, it seems intuitively accurate that pain in OA impacts mental health, and disentangling this connection is difficult (Tofferi et al., 2004). For example, even though we separated the independent variable from the result by one week in our analyses, individuals may have a premonition of pain they would feel the next week, which may impact their mental health. Although we attempted to establish the mental health variable as predictive in our study, the potential of reverse causality playing a major role in the findings cannot be ruled out (Arnold et al., 2004).

It's possible that, in the end, the issue of causation is academic. It's possible that an iterative mechanism is at work, with a continuous stream of OA pain and associated poor mental health that feeds back on itself over time. The cross-sectional correlation we discovered is certainly compatible with such a scenario (Arnold et al., 2005). It is worthwhile to examine if joining that process at any time with a therapeutic intervention linked to mental health will be able to stop the cyclical pain process. A number of variables, including social isolation, sleep alterations, and changes in physical activity, may all play a role in the connection between pain and mental health. Given the information gathered in the LEAP research, we were unable to investigate these issues (Nettles et al., 2005).

5. CONCLUSION

Finally, we found that reporting of poorer or deteriorating mental health predicts reporting of worse OA-related pain and OA pain flares. With the scarcity of effective OA pain treatments and the toxicity of those in widespread use, mental health may offer a new therapeutic focus for OA pain, with potentially substantial benefits for both patients and doctors.

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Ethical approval

The study was approved by the Medical Ethics Committee of KSUM University (ethical approval code: lkjhrf983093).

Conflicts of interest

The authors declare that they have no conflict of interest.

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Data and materials availability

All data associated with this study are present in the paper.

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